

tartaric acid

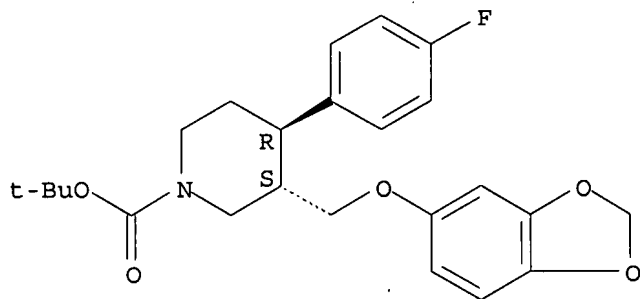
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of paroxetine hydrochloride propanol solvate via human metabolite intermediate and characterization of solvate crystals)

RN 200572-35-6 CAPLUS

CN 1-Piperidinecarboxylic acid, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, 1,1-dimethylethyl ester, (3S,4R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL CASREACT

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FILE CONTENT:1840 - 10 Nov 2007 VOL 147 ISS 21

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This file contains CAS Registry Numbers for easy and accurate substance identification.

tartaric acid

=> SET NOTICE DISPLAY 1

NOTICE SET TO 1 U.S. DOLLAR FOR DISPLAY COMMAND
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=> D ACC 133:4631 ALL

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ANSWER 1 CASREACT COPYRIGHT 2007 ACS on STN

AN 133:4631 CASREACT

TI Improved synthesis of paroxetine hydrochloride propan-2-ol solvate through one of metabolites in humans, and characterization of the solvate crystals

AU Sugi, Kiyoshi; Itaya, Nobushige; Katsura, Tadashi; Igi, Masami; Yamazaki, Shigeya; Ishibashi, Taro; Yamaoka, Teiji; Kawada, Yoshihiro; Tagami, Yayoi; Otsuki, Michiya; Ohshima, Takao

CS Central Research Laboratories, Sumika Fine Chemicals Co., Ltd., Osaka, 555-0021, Japan

SO Chemical & Pharmaceutical Bulletin (2000), 48(4), 529-536

CODEN: CPBTAL; ISSN: 0009-2363

PB Pharmaceutical Society of Japan

DT Journal

LA English

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1, 63

AB Paroxetine, a potent and selective inhibitor of 5-hydroxytryptamine (serotonin) uptake, was prepared through a piperidine derivative, which was reported to be one of the paroxetine metabolites in humans. Thus, the piperidine derivative was converted to its N-tert-butoxycarbonyl (N-Boc) derivative, which was then converted to N-Boc paroxetine. Paroxetine hydrochloride propan-2-ol (iso-Pr alc. (IPA)) solvate crystals were directly obtained from the N-Boc paroxetine by adding hydrogen chloride to the N-Boc paroxetine IPA solution. The amount of IPA content in the crystals was reduced by drying with a continuous change of powder X-ray diffraction patterns. Other characterizations of the solvate crystals were also conducted.

ST paroxetine Paxil prepn; propanol paroxetine hydrochloride prepn; hemihydrate paroxetine hydrochloride prepn

IT 78246-49-8P 110429-35-1P, Paroxetine hydrochloride hemihydrate 181237-68-3P, 2-Propanol compound with (3S,4R)-3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)piperidine hydrochloride

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (preparation of paroxetine hydrochloride propanol solvate via human metabolite intermediate and characterization of solvate crystals)

IT 105-34-0, Methyl cyanoacetate 459-57-4, 4-Fluorobenzaldehyde 533-31-3, 1,3-Benzodioxol-5-ol 34619-03-9, Di-tert-butyl carbonate 271595-66-5, Paroxetine L-o-chlorotartranilic acid salt

RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of paroxetine hydrochloride propanol solvate via human metabolite intermediate and characterization of solvate crystals)

IT 125224-43-3P, (3S,4R)-(-)-4-(4-Fluorophenyl)-3-piperidinemethanol 188869-26-3P, (3R,4S)-rel-4-(4-Fluorophenyl)-3-piperidinemethanol 200572-35-6P, (3S,4R)-3-[(1,3-Benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-1-piperidinecarboxylic acid 1,1-dimethylethyl ester 200572-36-7P, 2-Cyano-3-(4-fluorophenyl)pentanedioic acid dimethyl ester 200572-37-8P, (3R,4S)-rel-4-(4-Fluorophenyl)-6-oxo-3-piperidinecarboxylic acid methyl ester 200572-39-0P, 4-(4-Fluorophenyl)-6-oxo-3-piperidinecarboxylic acid methyl ester

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

tartaric acid

(Reactant or reagent)

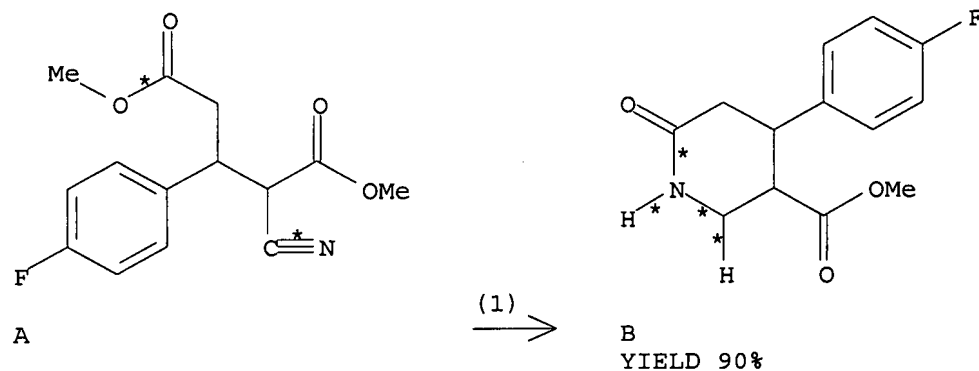
(preparation of paroxetine hydrochloride propanol solvate via human metabolite intermediate and characterization of solvate crystals)

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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- (9) Hansen, J; 1997 CAPLUS
- (10) Hansen, J; PCT Int Appl WO 96 36636 1996
- (11) Koelsch, C; J Am Chem Soc 1943, V65, P2459 CAPLUS
- (12) Montzka, T; J O Chem 1968, V33, P3393
- (13) Patil, V; Indian Drugs 1998, V35, P686 CAPLUS
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- (15) Sugi, K; Eur Pat Appl EP 812827 1997
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- (21) Yokota, M; Bull Chem Soc 1999, V72, P1731 CAPLUS

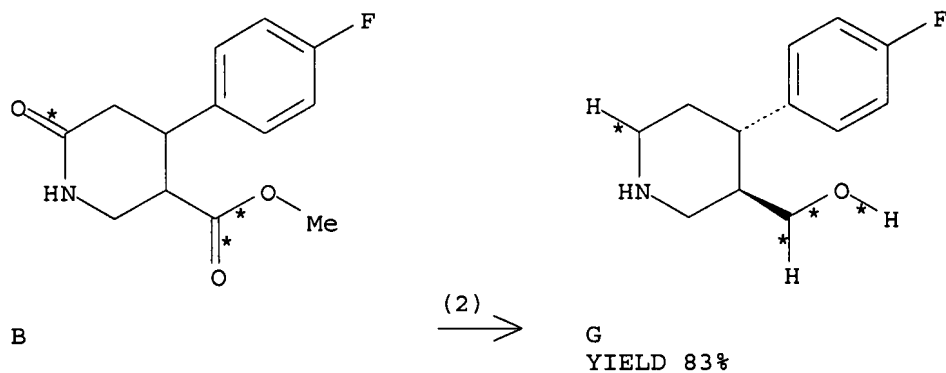
RX(1) OF 15 ...A ==> B...



RX(1) RCT A 200572-36-7
RGT C 1333-74-0 H2
PRO B 200572-39-0
CAT 7440-02-0 Ni
SOL 67-56-1 MeOH, 108-88-3 PhMe

RX(2) OF 15 ...B ==> G...

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RX(2) RCT B 200572-39-0

STAGE(1)

RGT H 124-41-4 NaOMe

SOL 108-88-3 PhMe

STAGE(2)

RGT I 16853-85-3 LiAlH₄

SOL 109-99-9 THF

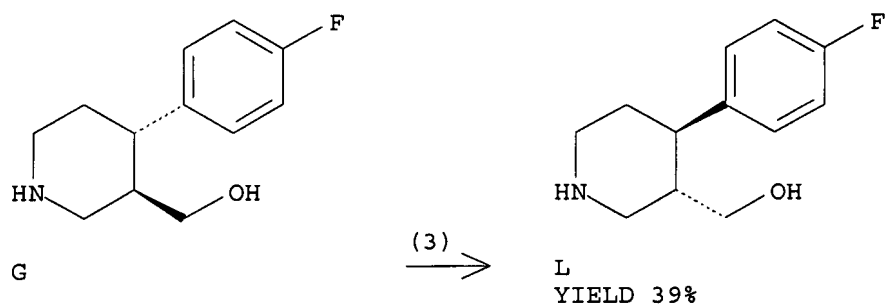
STAGE(3)

RGT J 1310-73-2 NaOH

PRO G 188869-26-3

NTE STEREOSELECTIVE

RX(3) OF 15 ...G ==> L...



RX(3) RCT G 188869-26-3

RGT M 17447-35-7 Butanoic acid, 4-[(4-chlorophenyl)amino]-2,3-dihydroxy-4-oxo-, (2R,3R)-

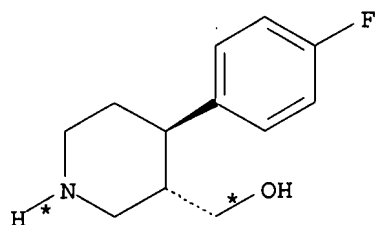
PRO L 125224-43-3

SOL 7732-18-5 Water

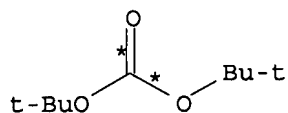
NTE STEREOSELECTIVE

RX(4) OF 15 ...L + O + P ==> Q

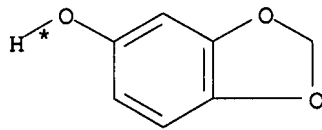
tartaric acid



L

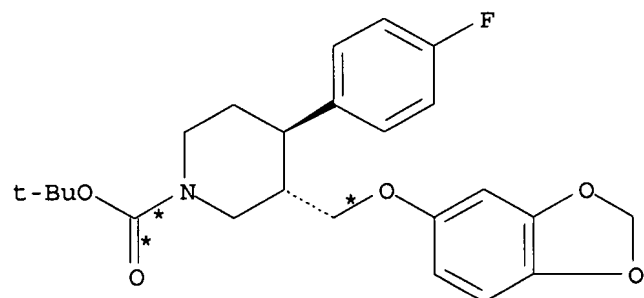


O



P

(4)
→



Q

YIELD 87%

RX(4) RCT L 125224-43-3, O 34619-03-9

STAGE(1)

RGT J 1310-73-2 NaOH

SOL 7732-18-5 Water, 108-88-3 PhMe

STAGE(2)

RGT R 121-44-8 Et3N, S 98-59-9 TsCl

SOL 108-88-3 PhMe

STAGE(3)

RCT P 533-31-3

RGT J 1310-73-2 NaOH, H 124-41-4 NaOMe

STAGE(4)

RGT T 7647-01-0 HCl, U 67-63-0 Me2CHOH

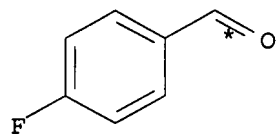
SOL 108-88-3 PhMe

PRO Q 200572-35-6

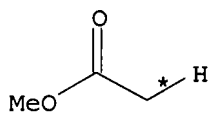
NTE STEREOSELECTIVE

RX(5) OF 15 V + W + X ==> A...

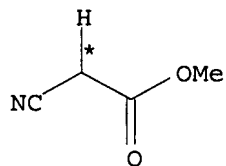
tartaric acid



V

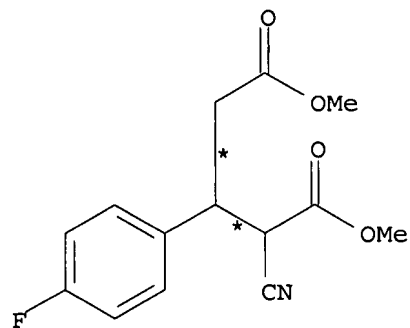


W



X

(5) →



A

YIELD 79%

RX(5) RCT V 459-57-4, W 79-20-9

STAGE(1)

RGT H 124-41-4 NaOMe

SOL 108-88-3 PhMe

STAGE(2)

RCT X 105-34-0

STAGE(3)

RGT T 7647-01-0 HCl

SOL 7732-18-5 Water

STAGE(4)

SOL 108-88-3 PhMe

PRO A 200572-36-7

tartaric acid

=> s paroxetine(1)buty?

3333 PAROXETINE

610983 BUTY?

L1 17 PAROXETINE(L)BUTY?

=> d bib hit 1-17

L1 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:965034 CAPLUS

DN 141:400958

TI Drug formulations with methacrylic acid-methylacrylate-ethylacrylate-butylmethacrylate copolymer containing coating or matrix

IN Petereit, Hans-Ulrich; Meier, Christian; Schultes, Klaus

PA Roehm G.m.b.H. & Co. K.-G., Germany

SO PCT Int. Appl., 47 pp.

CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004096185	A1	20041111	WO 2004-EP2061	20040302
	W:			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW	
	RW:			BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG	
	DE 10319458	A1	20041118	DE 2003-10319458	20030429
	CA 2489064	A1	20041111	CA 2004-2489064	20040302
	EP 1496870	A1	20050119	EP 2004-716230	20040302
	R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK	
	BR 2004003949	A	20050301	BR 2004-3949	20040302
	CN 1697649	A	20051116	CN 2004-80000276	20040302
	JP 2006524643	T	20061102	JP 2006-504498	20040302
	IN 2004CN02444	A	20070907	IN 2004-CN2444	20040827
	US 2005152977	A1	20050714	US 2004-512860	20041115
PRAI	DE 2003-10319458	A	20030429		
	WO 2004-EP2061	W	20040302		

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 50-23-7, Hydrocortisone 50-24-8, Prednisolone 50-48-6, Amitriptyline 50-52-2, Thioridazine 50-78-2, Acetylsalicylic acid 50-81-7, L-Ascorbic acid, biological studies 52-53-9, Verapamil 53-86-1, Indometacin 54-31-9, Furosemide 55-63-0, Glycerol trinitrate 56-54-2, Quinidine 57-27-2, Morphin, biological studies 58-55-9, Theophylline, biological studies 67-20-9, Nitrofurantoin 70-47-3, Aspartamic acid, biological studies 71-63-6, Digitoxin 87-33-2, Isosorbide dinitrate 89-57-6, 5-Aminosalicylic acid 99-66-1, Valproic acid 100-97-0, biological studies 103-90-2, Paracetamol 113-92-8 130-95-0, Quinine 151-21-3, Sodium lauryl sulfate, biological studies 153-18-4, Rutoside 155-97-5, Pyridostigmine 298-46-4, Carbamazepin 315-30-0, Allopurinol 317-34-0, Aminophyllin 364-62-5, Metoclopramide 437-74-1, Xantinolnicotinate 479-92-5, Propyphenazone 525-66-6, Propranolol 599-79-1, Sulfasalazin 604-75-1, Oxazepam 1200-22-2,

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Lipoic acid 1310-73-2, Sodium hydroxide, biological studies 2179-37-5, Bencyclane 2530-97-4, Xanthinol 2809-21-4 3737-09-5, Disopyramide 4498-32-2, Dibenzepine 4499-40-5, Choline theophyllinate 5104-49-4, Flurbiprofen 5636-83-9, Dimetindene 6452-71-7, Oxprenolol 6493-05-6, Pentoxifylline 6805-41-0, Aescin 7439-93-2, Lithium, biological studies 7439-93-2D, Lithium, salts 7440-09-7, Potassium, biological studies 7440-09-7D, Potassium, salts 7440-23-5, Sodium, biological studies 7440-23-5D, Sodium, salts 7440-66-6, Zinc, biological studies 7440-66-6D, Zinc, salts 7681-49-4, Sodium fluoride, biological studies 7681-93-8, Natamycin 8049-47-6, Pancreatin 9002-07-7, Trypsin 9002-64-6, Parathormone 9002-72-6, Somatotropin 9004-10-8, Insulin, biological studies 9006-65-9, Dimethicone 9007-12-9, Calcitonin 9007-92-5, Glucagon, biological studies 10596-23-3 11000-17-2, Vasopressin 13523-86-9, Pindolol 14838-15-4, Norephedrine 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 16051-77-7, Isosorbide mononitrate 16110-51-3, Cromolyn 16662-47-8, Gallopamil 16679-58-6 18559-94-9, Salbutamol 18683-91-5, Ambroxol 21829-25-4, Nifedipine 22071-15-4, Ketoprofen 22204-53-1, Naproxen 23031-25-6, Terbutalin 25717-80-0, Molsidomine 25812-30-0, Gemfibrozil 27203-92-5, Tramadol 29122-68-7, Atenolol 31329-57-4, Naftidrofuryl 40391-99-9 41575-94-4, Carboplatin 41859-67-0, Bezafibrate 42399-41-7, Diltiazem 49562-28-9, Fenofibrate 51110-01-1, Somatostatin 51333-22-3, Budesonide 51384-51-1, Metoprolol 53808-88-1, Lonazolac 55837-25-7, Buflomedil 55837-27-9, Piretanide 55985-32-5, Nicardipine 57132-53-3, Proglumetacin 61869-08-7, Paroxetine 63675-72-9, Nisoldipine 66085-59-4, Nimodipine 66376-36-1, Alendronate 73590-58-6, Omeprazole 74381-53-6, Leuprolide acetate 75330-75-5, Lovastatin 77337-73-6, Acamprosate calcium 79902-63-9, Simvastatin 81093-37-0, Pravastatin 88150-42-9, Amlodipine 89662-30-6, Detirelix 93413-69-5, Venlafaxine 93957-54-1, Fluvastatin 98530-12-2, Intron A 102625-70-7, Pantoprazole 103577-45-3 114084-78-5, Ibandronate 117976-89-3, Rabeprazole 119141-88-7, Esomeprazole 120287-85-6, Cetorelix 134523-00-5, Atorvastatin 143011-72-7, Granulocyte Colony Stimulating factor 145599-86-6, Cerivastatin 150977-36-9, Bromelain 161973-10-0, Perprazole

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(drug formulations with methacrylic acid-methylacrylate-ethylacrylate-butylmethacrylate copolymer containing coating or matrix)

L1 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:299547 CAPLUS

DN 140:331639

TI Trends in the development of new antidepressants. Is there a light at the end of the tunnel?

AU Pacher, Pal; Kecskemeti, Valeria

CS National Institute on Alcohol Abuse & Alcoholism, Laboratory of Physiologic Studies, National Institutes of Health, Rockville, MD, 20852, USA

SO Current Medicinal Chemistry (2004), 11(7), 925-943
CODEN: CMCHE7; ISSN: 0929-8673

PB Bentham Science Publishers Ltd.

DT Journal; General Review

LA English

RE.CNT 226 THERE ARE 226 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB A review. Since the introduction of tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) in mid-1950's, treatment of depression was dominated by monoamine hypotheses. The well-established clin. efficacy of TCAs and MAOIs is due, at least in part, to the enhancement of noradrenergic or serotonergic mechanisms, or to both. Unfortunately, their very broad mechanisms of action also include many unwanted effects related to their potent activity on cholinergic,

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adrenergic, and histaminergic receptors. The introduction of selective serotonin reuptake inhibitors (SSRIs) over twenty years ago had been the next major step in the evolution of antidepressants to develop drugs as effective as the TCAs but of higher safety and tolerability profile. During the past 2 decades SSRIs (fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram) gained incredible popularity and have become the most widely prescribed medication in the psychiatric practice. The evolution of antidepressants continued resulting in introduction of selective and reversible monoamine oxidase inhibitors (eg. moclobemid), selective noradrenaline (eg. reboxetine), dual noradrenaline and serotonin reuptake inhibitors (milnacipram, venlafaxin, duloxetine) and drugs with distinct neurochem. profiles such as mirtazapine, nefazadone, and tianeptine. Different novel serotonin receptor ligands were also intensively investigated. In spite of the remarkable structural diversity, most currently introduced antidepressants are "monoamine based". Furthermore, these newer agents are neither more efficacious nor rapid acting than their predecessors and approx. 30% of the population do not respond to current therapies. By the turn of the new millennium, the authors are all witnessing a result of innovative developmental strategies based on the better understanding of pathophysiol. of depressive disorder. Several truly novel concepts have emerged suggesting that the modulation of neuropeptide (substance P, corticotrophin-releasing factor, neuropeptide Y, vasopressin V1b, melanin-concentrating hormone-1), N-methyl-D-aspartate, nicotinic acetylcholine, dopaminergic, glucocorticoid, δ -opioid, cannabinoid and cytokine receptors, gamma-amino butyric acid (GABA) and intracellular messenger systems, transcription, neuroprotective and neurogenic factors, may provide an entirely new set of potential therapeutic targets, giving hope that further major advances might be anticipated in the treatment of depressive disorder soon. The goal of this review is to give a brief overview of the major advances from monoamine-based treatment strategies, and particularly focus on the new emerging approaches in the treatment of depression.

L1 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:111462 CAPLUS

DN 141:348856

TI Resolution of paroxetine precursor using different lipases Influence of the reaction conditions on the enantioselectivity of lipases

AU Fernandez-Lorente, Gloria; Palomo, Jose M.; Mateo, Cesar; Guisan, Jose M.; Fernandez-Lafuente, Roberto

CS Department of Biocatalysis, CSIC, Institute of Catalysis, Madrid, 28049, Spain

SO Enzyme and Microbial Technology (2004), 34(3-4), 264-269
CODEN: EMTED2; ISSN: 0141-0229

PB Elsevier Science

DT Journal

LA English

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB In this manuscript, lipases from different sources have been evaluated in the resolution of (+)-(4RS,5RS)-trans-5-(butyryloxymethyl)-4-(4'-fluorophenyl)-1-methyl-piperidin-2-one, an interesting precursor of paroxetine. Three of the analyzed lipases [*Pseudomonas fluorescens* (PFL), *Candida antarctica* form B (CAL-B) and *Aspergillus oryzae* (AOL)] were selected for having the highest specific activity. It was found that slight changes on the reaction conditions greatly altered the lipases properties; for example the E value for PFL immobilized on octyl-Sepharose improved from 2 to 25 just by adding some organic solvent, being the (+)-trans-1 the preferred isomer. Moreover, the E value for the com. preparation of CAL-B could be altered from 2 to 18, favoring the (+)-trans-1 isomer. In the case of AOL, the E value could be improved

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from 3.5 to 16 in the presence of 20% dioxane. It is remarkable that this lipase presented the reverse enantioference compared to the other two lipases. Thus, good enantioselectivities could be achieved with the three enzymes, just by an appropriate engineering of the reaction medium.

L1 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2003:492188 CAPLUS

DN 139:77878

TI Preparation of tropanes, their rhenium and technetium chelates and use as radiopharmaceuticals and diagnostic agents

IN Turpin, Frederic; Mauclaire, Laurent; Masri, Fadi; Riche, Francoise; Du Moulinet D'Hardemare, Amaury

PA Schering Aktiengesellschaft, Germany

SO Fr. Demande, 65 pp.

CODEN: FRXXBL

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2833952	A1	20030627	FR 2001-16867	20011226
	FR 2833952	B1	20040326		
	WO 2003055879	A2	20030710	WO 2002-IB5357	20021213
	WO 2003055879	A3	20040617		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002367114	A1	20030715	AU 2002-367114	20021213
PRAI	FR 2001-16867	A	20011226		
	WO 2002-IB5357	W	20021213		

OS MARPAT 139:77878

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The present invention concerns tropanes (shown as I; variables defined below; e.g. II), their metal chelates with rhenium and technetium (e.g. Tc oxo and nitrido complexes with II), methods of preparation of the tropanes and their chelates, and uses as radiopharmaceuticals and diagnostic agents, e.g. visualization of reuptake of dopamine or serotonin. For I: X = a compound of chelation of a metal or a metal complex, carbons 6 and 7 being bonded or not; R1 is an alkyl or a alkenyl; R2 is COOZ (Z = H, alkyl); R3 = Ph, phenylalkyl or phenylalkenyl, benzoate or oxo; the connection between carbons 2 and 3 is a simple or double bond. The portions of X bonded to carbons 6 and 7 may be, for example, :NN(R7)CS2Me (R7 = H, Me). For example, II was prepared in a multistep synthesis starting from N-Bocpyrrole and (1S)-2-ethoxy-1-methyl-2-oxoethyl 3-(tert-butylidimethylsiloxy)-2-diazo-3-oxo-3-butenate (prepn. described) involving the following intermediates: (1S)-2-ethoxy-1-methyl-2-oxoethyl (1R,5R)-8-[(1,1-dimethylethoxy)carbonyl]-3-(tert-butylidimethylsiloxy)-8-azabicyclo[3.2.1]octa-2,6-diene-2-carboxylate (shown as III, 75%), (1S)-2-ethoxy-1-methyl-2-oxoethyl (1R,5R)-8-[(1,1-dimethylethoxy)carbonyl]-8-azabicyclo[3.2.1]oct-6-en-3-one-2-carboxylate, (1S)-2-ethoxy-1-methyl-2-oxoethyl (1R,5R)-8-[(1,1-dimethylethoxy)carbonyl]-3-(trifluoromethanesulfonyloxy)-8-azabicyclo[3.2.1]octa-2,6-diene-2-carboxylate (22%), (1S)-2-ethoxy-1-methyl-2-oxoethyl (1R,5R)-8-[(1,1-dimethylethoxy)carbonyl]-3-(p-tolyl)-8-

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azabicyclo[3.2.1]octa-2,6-diene-2-carboxylate (33%), Me (1R,5R)-8-[(1,1-dimethylethoxy)carbonyl]-3-(p-tolyl)-8-azabicyclo[3.2.1]octa-2,6-diene-2-carboxylate (95%), Me (1R,2R,3R,5R)-8-[(1,1-dimethylethoxy)carbonyl]-3-(p-tolyl)-8-azabicyclo[3.2.1]oct-6-ene-2-carboxylate (85%), Me (1R,2R,3R,5R,6R,7R)-8-[(1,1-dimethylethoxy)carbonyl]-6,7-dihydroxy-3-(p-tolyl)-8-azabicyclo[3.2.1]octane-2-carboxylate (99%), and Me (1R,2R,3R,5R)-6-[(1,1-dimethylethoxy)carbonyl]-1,5-diformyl-3-(p-tolyl)-6-azacyclohexane-2-carboxylate (70%). Pharmacol. testing of Tc complexes of tropane derivs. yielded the following results: preinjection of GBR 12909 (specific inhibitor of dopamine transport) in rats prevented their fixation in the striatum; in vitro competitive studies on cerebral membranes with radiolabeled GBR 12925, paroxetine and nisoxetine showed the Tc complexes to have good affinity and specificity for dopamine transport; in vivo kinetic studies of cerebral distribution in a primate shows the complexes to be useful for visualization of dopamine transport; they pass the hemato-encephalic barrier and accumulate preferentially in the striatum with an elevated striatum/cerebellum ratio.

L1 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2003:58812 CAPLUS

DN 138:122554

TI Enzymic resolution of trans-4-(4-fluorophenyl)-3-hydroxymethylpiperidine derivative for optically pure paroxetine precursors

IN Bayod Jasanada, Miguel; Sanchez Pedregal, Victor; Gotor Santamaria, Vicente; Brieva Collado, Rosario; De Gonzalo Calvo, Gonzalo

PA Astur Pharma, Spain

SO U.S. Pat. Appl. Publ., 9 pp.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	US 2003018048	A1	20030123	US 2002-192768	20020710
	ES 2194588	A1	20031116	ES 2001-1648	20010713
	ES 2194588	B1	20041016		
	EP 1283200	A2	20030212	EP 2002-380156	20020710
	EP 1283200	A3	20030305		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

PRAI ES 2001-1648 A 20010713

OS CASREACT 138:122554; MARPAT 138:122554

IT 108-88-3, Toluene, uses 141-78-6, Ethyl acetate, uses 1634-04-4, tert-Butyl methyl ether

RL: NUU (Other use, unclassified); USES (Uses)
(reaction solvent; enzymic resolution of trans(4-fluorophenyl)hydroxymethylpiperidine derivative for optically pure paroxetine precursors)

L1 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2003:28518 CAPLUS

DN 138:314796

TI Fox odor affects corticosterone release but not hippocampal serotonin reuptake and open-field behavior in rats

AU Dias Soares, Danusa; Fernandez, Francesca; Aguerre, Sylvie; Foury, Aline; Mormede, Pierre; Chaoulloff, Francis

CS INSERM U471-INRA, Institut F. Magendie, Bordeaux, 33077, Fr.

SO Brain Research (2003), 961(1), 166-170
CODEN: BRREAP; ISSN: 0006-8993

PB Elsevier Science B.V.

DT Journal

tartaric acid

LA English

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Group-housed Sprague-Dawley (SD) rats exposed for 1 h to 2,5-dihydro-2,4,5-trimethylthiazoline (TMT, a component of fox feces) did not display changes in hippocampal serotonin (5-HT) metabolism and [3H]5-HT reuptake, compared to water or butyric acid. Such an observation extended to isolated SD and Fischer 344 rats. When group-housed SD rats were tested 1 wk after a 1-h exposure to TMT, hippocampal 5-HT metabolism, [3H]5-HT reuptake, and [3H]paroxetine binding at the 5-HT transporter remained unchanged. This study questions TMT as a specific predatory stimulus as both butyric acid and TMT increased plasma corticosterone levels while leaving intact open-field behavior (at least in group-housed SD rats).

L1 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2002:676014 CAPLUS

DN 137:216939

TI Process of preparing paroxetine and intermediates for use therein

IN Callewaert, George Leo

PA Spurcourt Limited, UK

SO PCT Int. Appl., 67 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002068416	A2	20020906	WO 2002-GB771	20020222
	WO 2002068416	A3	20021121		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	CA 2438892	A1	20020906	CA 2002-2438892	20020222
	AU 2002232017	A1	20020912	AU 2002-232017	20020222
	EP 1362032	A2	20031119	EP 2002-712110	20020222
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
	US 2004073038	A1	20040415	US 2003-468865	20030820
PRAI	GB 2001-4583	A	20010224		
	GB 2001-25119	A	20011018		
	WO 2002-GB771	W	20020222		
OS	MARPAT 137:216939				
IT	501-53-1, Benzyl chloroformate	24424-99-5, Di-tert-butyl dicarbonate	66270-36-8, 2,2,2-Trichloro-1,1-dimethylethyl chloroformate		
	RL: RCT (Reactant); RACT (Reactant or reagent)				
	(acylation agent; process of preparing paroxetine and intermediates for use therein)				
IT	74-89-5, Methylamine, reactions	75-04-7, Ethylamine, reactions			
	100-46-9, Benzylamine, reactions	104-84-7, 4-Methylbenzylamine			
	105-53-3, Diethyl malonate	109-73-9, Butylamine, reactions			
	109-85-3, 2-Methoxyethylamine	4795-29-3, Tetrahydrofurfurylamine			
	RL: RCT (Reactant); RACT (Reactant or reagent)				
	(preparation of starting materials; process of preparing paroxetine and intermediates for use therein)				

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L1 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2002:310324 CAPLUS

DN 136:380004

TI Prolonged prenatal psychotropic medication exposure alters Neonatal acute pain response

AU Oberlander, Tim F.; Grunau, Ruth Eckstein; Fitzgerald, Colleen; Ellwood, Ann-Louise; Misri, Shaila; Rurak, Dan; Riggs, Kenneth Wayne

CS Department of Pediatrics, University of British Columbia, Vancouver, BC, V6H 3V4, Can.

SO Pediatric Research (2002), 51(4), 443-453

CODEN: PEREBL; ISSN: 0031-3998

PB Lippincott Williams & Wilkins

DT Journal

LA English

RE.CNT 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Selective serotonin reuptake inhibitors (SSRIs) and benzodiazepines are frequently used to treat maternal depression during pregnancy, however the effect of increased serotonin (5HT) and γ -amino- butyric acid (GABA) agonists in the fetal human brain remains unknown. 5HT and GABA are active during fetal neurol. growth and play early roles in pain modulation, therefore, if prolonged prenatal exposure alters neurodevelopment this may become evident in altered neonatal pain responses. To examine biol. and behavioral effects of prenatal exposure, neonatal responses to acute pain (phenylketonuria heel lance) in infants with prolonged prenatal exposure were examined. Facial action (Neonatal Facial Coding System) and cardiac autonomic reactivity derived from the relationship between respiratory activity and short term variations of heart rate (HRV) were compared between 22 infants with SSRI exposure (SE) [fluoxetine (n = 7), paroxetine (n = 11), sertraline (n = 4)]; 16 infants exposed to SSRIs and clonazepam (SE+) [paroxetine (n = 14), fluoxetine (n = 2)]; and 23 nonexposed infants during baseline, lance, and recovery periods of a heel lance. Length of maternal SSRI use did not vary significantly between exposure groups-[mean (range)] SE:SE+ 183 (31-281):141 (54-282) d (p > 0.05). Infants exposed to SE and SE+ displayed significantly less facial activity to heel lance than control infants. Mean HR increased with lance, but was significantly lower in SE infants during recovery. Using measures of HRV and the transfer relationship between heart rate and respiration, SSRI infants had a greater return of parasympathetic cardiac modulation in the recovery period, whereas a sustained sympathetic response continued in the control group. Prolonged prenatal SSRI exposure appears to be associated with reduced behavioral pain responses and increased parasympathetic cardiac modulation in recovery following an acute neonatal noxious event. Possible 5HT-mediated pain inhibition, pharmacol. factors and the developmental course remain to be studied.

L1 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2000:240402 CAPLUS

DN 133:4631

TI Improved synthesis of paroxetine hydrochloride propan-2-ol solvate through one of metabolites in humans, and characterization of the solvate crystals

AU Sugi, Kiyoshi; Itaya, Nobushige; Katsura, Tadashi; Igi, Masami; Yamazaki, Shigeya; Ishibashi, Taro; Yamaoka, Teiji; Kawada, Yoshihiro; Tagami, Yayoi; Otsuki, Michiya; Ohshima, Takao

CS Central Research Laboratories, Sumika Fine Chemicals Co., Ltd., Osaka, 555-0021, Japan

SO Chemical & Pharmaceutical Bulletin (2000), 48(4), 529-536

CODEN: CPBTAL; ISSN: 0009-2363

PB Pharmaceutical Society of Japan

DT Journal

LA English

tartaric acid

OS CASREACT 133:4631

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 105-34-0, Methyl cyanoacetate 459-57-4, 4-Fluorobenzaldehyde 533-31-3,
1,3-Benzodioxol-5-ol 34619-03-9, Di-tert-butyl carbonate
271595-66-5, Paroxetine L-o-chlorotartranilic acid salt

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of paroxetine hydrochloride propanol solvate via
human metabolite intermediate and characterization of solvate crystals)

L1 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1999:94050 CAPLUS

DN 130:320701

TI Psychopharmacological profile of the selective serotonin reuptake
inhibitor, paroxetine: implication of noradrenergic and serotonergic
mechanisms

AU Redrobe, John P.; Bourin, Michel; Colombel, Marie Claude; Baker, Glen B.
CS GIS Medicament, JE 2027 Neurobiologie de l'anxiete, Faculte de Medecine,
Nantes, 44035, Fr.

SO Journal of Psychopharmacology (London) (1998), 12(4), 348-355
CODEN: JOPSEQ; ISSN: 0269-8811

PB SAGE Publications

DT Journal

LA English

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The present study was designed to evaluate the psychopharmacol. profile of
the selective serotonin reuptake inhibitor paroxetine, and thus
assess potential noradrenergic and/or serotonergic activity.
Paroxetine dose-dependently increased mobility time in the mouse
forced swimming test (8, 16, 32 and 64 mg/kg, i.p.) and reduced
spontaneous locomotor activity when administered at a high dose (64 mg/kg,
i.p.). Prior administration of 8-hydroxy-2-(di-n-propylamino)tetralin (1
mg/kg, i.p.), (+) pindolol (32 mg/kg, i.p.) or 5-methoxy-3-(1,2,3,6-
tetrahydro-4-pyridyl)-1H-indole (RU 24969) (1 mg/kg, i.p.) potentiated the
antidepressant-like effects of subactive doses of paroxetine (1,
2 and 4 mg/kg, i.p.) in the mouse forced swimming test. These effects
were antagonized by prior administration of 1-(2-methoxyphenyl)-4-[-(2-
phthalimido)butyl]piperazine) (0.5 mg/kg, i.p.). Complementary
studies suggested that RU24969-induced anti-immobility effects were a
result of an increase in locomotor activity; other interactions were
without increase/decrease in locomotor activity. Acute administration of
paroxetine (8, 16, and 32 mg/kg, i.p.) antagonized the hypothermia
induced by the D2/D1 receptor agonist, apomorphine (16 mg/kg, s.c.), while
repeated treatment with paroxetine (32 mg/kg) attenuated
clonidine-induced (0.5 mg/kg, i.p.) hypothermia. Pre-treatment with the
serotonergic neurotoxin, para-chlorophenylalanine attenuated the
anti-immobility effects of low doses of paroxetine (8 and 16
mg/kg, i.p.) in the forced swimming test, whereas a higher dose of
paroxetine remained active (32 mg/kg, i.p.). The results of the
present study indicated that paroxetine displayed both
noradrenergic-like and serotonergic-like activity in the pre-clin.
psychopharmacol. tests employed.

L1 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1999:74285 CAPLUS

DN 130:261951

TI N-tert-butyl-alpha-phenylnitrone protects against 3,4-
methylenedioxymethamphetamine-induced depletion of serotonin in rats

AU Yeh, S. Y.

CS Molecular Neuropsychiatry Section, Intramural Research Program, National
Institute on Drug Abuse, National Institutes of Health, Baltimore, MD,

tartaric acid

21224, USA

SO Synapse (New York) (1999), 31(3), 169-177

CODEN: SYNAET; ISSN: 0887-4476

PB Wiley-Liss, Inc.

DT Journal

LA English

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The present study examined the effect of N-tert-butyl
-alpha-phenylnitron (PBN) on 3,4-methylenedioxymethamphetamine
(MDMA)-induced depletion of serotonin in the CNS. Rats were treated with
two concurrent injections of MDMA (20 mg/kg, s.c.), PBN (50-400 mg/kg
dissolved in ethanol, 50 mg/mL of 25% ethanol, i.p.), saline or 25%
ethanol, alone or in combination, 6 h apart, and sacrificed 5 days later.
Rectal temperature was measured prior to and hourly following the drug
injection

for 5 h. Monoamine levels in the tissue were measured by HPLC. D. of the
5-HT transporters was assayed by [3H]paroxetine binding. Rectal
temperature of rats increased after MDMA, decreased after PBN, ethanol, PBN

plus

ethanol, and MDMA plus ethanol, and was not significantly altered after
MDMA plus PBN. Levels of 5-HT and 5-HIAA in the frontal cortex,
hippocampus, striatum, and brain stem of rats decreased significantly
after MDMA or MDMA plus ethanol, but not after MDMA plus PBN, PBN plus
ethanol (PBN dissolved in ethanol), or ethanol as compared to the saline
controls. Levels of 5-HT and 5-HIAA in the brain tissues of rats treated
with MDMA plus PBN were elevated as compared to those treated with MDMA
plus saline. Similar results were observed in the d. of 5-HT transporters in
the frontal cortex and hippocampus. These results indicate that
scavenging of free radicals of MDMA metabolites or reactive oxygen species
by PBN and with lowering of body temperature protected against MDMA-induced
depletion of serotonin transmitter.

L1 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1998:579448 CAPLUS

DN 130:371

TI Discriminative stimulus properties of the 5-HT1A receptor agonist BAY x
3702 in the rat

AU De Vry, Jean; Jentzsch, Klaus Rudiger

CS CNS Research, Bayer, Cologne, D-51063, Germany

SO European Journal of Pharmacology (1998), 357(1), 1-8

CODEN: EJPHAZ; ISSN: 0014-2999

PB Elsevier Science B.V.

DT Journal

LA English

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The aminomethylchroman derivative BAY x 3702 (R-(-)-2-{4-[(chroman-2-ylmethyl)-
amino]-butyl}-1,1-dioxo-benzo[d]isothiazolone HCl) has recently
been characterized as a relatively selective, high affinity 5-HT1A
receptor agonist with neuroprotective, anxiolytic- and antidepressant-like
effects in animal models. It was the aim of the present study to further
confirm its receptor binding profile in an in vivo assay. Rats were
trained to discriminate BAY x 3702 (0.1 mg/kg, i.p.) from vehicle in a
standard two-lever fixed ratio 10 food-reinforced procedure. All rats learned
the discrimination, the median number of sessions to reach criterion being 38
(range: 22-58 sessions). Generalization tests with BAY x 3702 showed
dose-dependent and complete generalization after different routes of
administration; the ED50 values being: 0.030, 0.007 and 0.36 mg/kg, after
i.p., i.v. and p.o. administration, resp. Assessment of the duration of
action after administration of 0.1 mg/kg BAY x 3702, i.p., resulted in a
T1/2 of 65 min. Dose-dependent and complete generalization was also

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obtained with the 5-HT_{1A} receptor agonists 8-OH-DPAT (8-hydroxy-2-(di-n-propylamino)-tetralin, ED₅₀ in mg/kg, i.p.: 0.086), flesinoxan (0.30), SR 57746A (4-(3-trifluoromethylphenyl)-N-(2-(naphth-2-yl)ethyl)-1,2,3,6-tetrahydropyridine HCl, 1.0), the (+)-enantiomer of BAY x 3702 (1.3) and ipsapirone (1.8); the ED₅₀ values being closely correlated with their resp. affinities for the 5-HT_{1A} receptor. Pretreatment with the selective 5-HT_{1A} receptor antagonist WAY-100635 ((N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-N(2-pyridinyl) cyclohexane carboxamide trihydrochloride) dose-dependently and completely blocked the discriminative effects of 0.1 mg/kg BAY x 3702 (ID₅₀: 0.013 mg/kg, i.p.). WAY-100635, prazosin, idazoxan, raclopride, paroxetine, (-)-BAY k 8644 (methyl-1,4-dihydro-2,6-dimethyl-3-nitro-4-(2-trifluoro-methyl-phenyl)-pyridine-5-carboxylate), ethanol, and the putative neuroprotectants MK-801 ((+)-5-methyl-10,11-dihydroxy-5H-dibenzo(a,d)cyclohepten-5,10-imine), CNS 1102 (N-(1-naphthyl)-N'-(3-ethylphenyl)-N'-methyl-guanidine), CGS 19755 (cis-4-(phosphonomethyl)piperidine-2-carboxylic acid) and nimodipine did not induce more than 20% generalization. It is concluded that the BAY x 3702 cue is mediated by its agonistic activity at 5-HT_{1A} receptors.

L1 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1998:250464 CAPLUS

DN 129:12626

TI Pindolol does not act only on 5-HT_{1A} receptors in augmenting antidepressant activity in the mouse forced swimming test

AU Bourin, Michel; Redrobe, John P.; Baker, Glen B.

CS GIS Medicament, JE 2027 Neurobiologie de l'Anxiete, Faculte de Medicine, Nantes, F-44035, Fr.

SO Psychopharmacology (Berlin) (1998), 136(3), 226-234

CODEN: PSCHDL; ISSN: 0033-3158

PB Springer-Verlag

DT Journal

LA English

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The present study was undertaken to identify the receptor subtypes involved in (±) pindolol's ability to enhance the effects of antidepressant drugs in the mouse forced swimming test. Interaction studies were performed with S 15535 (presynaptic 5-HT_{1A} receptor agonist) and methiothepin (5-HT_{1B} autoreceptor antagonist) to attenuate or potentiate antidepressant-like activity. (±) Pindolol was tested in combination with selective agonists and antagonists at 5-HT₁, 5-HT₂ and 5-HT₃ receptor subtypes. Pretreatment with S 15535 and methiothepin attenuated the activity of paroxetine, fluvoxamine and citalopram (32 mg/kg, IP; P < 0.01). (±) Pindolol (32 mg/kg, IP) induced significant anti-immobility effects when tested in combination with 5-methoxy-3-(1,2,3,6-tetrahydro-4-pyridyl)-1H-indole (RU 24969) (1 mg/kg, IP; P < 0.05), 1-(2-methoxyphenyl)-4-[-(2-phthalimido)butyl]piperazine (NAN 190) (0.5 mg/kg; P < 0.05) and ondansetron (0.00001 mg/kg, IP; P < 0.01). Pretreatment with NAN 190 (0.5 mg/kg, IP) potentiated the effects of RU 24969 (1 mg/kg, IP; P < 0.05) and (±) pindolol (32 mg/kg, IP; P < 0.05) in the forced swimming test, as did ondansetron (0.00001 mg/kg, IP). Significant additive effects were induced when RU 24969 (1 mg/kg, IP) was tested in combination with NAN 190 (0.5 mg/kg, IP; P < 0.05), (±) pindolol (32 mg/kg, IP; P < 0.05) and ondansetron (0.0000 mg/kg, IP; P < 0.05). 8-Hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT) (1 mg/kg, IP) or ketanserin (8 mg/kg, IP) did not induce significant antidepressant-like effects with any of the agonists/antagonists tested. The results of the present study suggest that pindolol is acting at presynaptic 5-HT_{1B} serotonergic receptors, in addition to the 5-HT_{1A} subtype, in augmenting the activity of antidepressants in the mouse forced swimming test.

tartaric acid

L1 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1998:13682 CAPLUS

DN 128:75308

TI Preparation of piperidine derivative as intermediates for the preparation of paroxetine

IN Sugi, Kiyoshi; Itaya, Nobushige; Katsura, Tadashi; Igi, Masami; Yamazaki, Shigeya; Ishibashi, Taro; Yamaoka, Teiji; Kawada, Yoshihiro; Tagami, Yayoi

PA Sumika Fine Chemicals Co., Ltd., Japan

SO Eur. Pat. Appl., 37 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	EP 812827	A1	19971217	EP 1997-303647	19970529
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL, SE				
	JP 10291975	A	19981104	JP 1997-145833	19970519
	JP 3819532	B2	20060913		
	EP 1384711	A1	20040128	EP 2003-77856	19970529
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL, SE				
	EP 1384720	A1	20040128	EP 2003-77858	19970529
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL, SE				
	EP 1394160	A1	20040303	EP 2003-77857	19970529
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL, SE				
IN	1997MA01172	A	20050304	IN 1997-MA1172	19970602
US	5948914	A	19990907	US 1998-53653	19980402
US	6476227	B1	20021105	US 2000-550175	20000414
US	6610851	B1	20030826	US 2000-695383	20001025
US	2003144519	A1	20030731	US 2003-336678	20030106
US	6815548	B2	20041109		
PRAI	JP 1996-175893	A	19960613		
	JP 1996-294585	A	19961015		
	JP 1996-303838	A	19961029		
	JP 1996-326177	A	19961120		
	JP 1997-50980	A	19970218		
	EP 1997-303647	A3	19970529		
	US 1997-871948	A3	19970610		
	US 1999-306411	B3	19990506		
	US 2000-695383	A3	20001025		

OS MARPAT 128:75308

IT 105-34-0, Methyl cyanoacetate 124-63-0, Methanesulfonyl chloride
459-57-4, p-Fluorobenzaldehyde 501-53-1, Benzyl chloroformate
533-31-3, 3,4-Methylenedioxyphenol 24424-99-5, Di-tert-butyl
dicarbonate 96426-60-7, Methyl p-fluorocinnamate 109887-53-8
125224-43-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of piperidine derivative as intermediates for the preparation

of

paroxetine)

L1 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1996:215542 CAPLUS

DN 125:11185

TI Synthesis of homochiral piperidine derivatives from S-glutamic acid.
Stereoselective 1,4-addition of organocuprates to a Δ^3 -piperidine-2-one. A paroxetine analog

AU Herdeis, Claus; Kaschinski, Claudia; Karia, Rolf; Lotter, Hermann

CS Inst. Pharmazie Lebensmittelchemie Univ., Wuerzburg, 97074, Germany

SO Tetrahedron: Asymmetry (1996), 7(3), 867-84

CODEN: TASYE3; ISSN: 0957-4166

tartaric acid

PB Elsevier
DT Journal
LA English
OS CASREACT 125:11185
IT 352-13-6, 4-Fluorophenylmagnesium bromide 591-51-5, Phenyllithium
693-03-8, Butylmagnesium bromide 873-77-8,
4-Chlorophenylmagnesium bromide 917-64-6, Methylmagnesium iodide
1730-25-2, Allylmagnesium bromide 10467-10-4, Ethylmagnesium iodide
20850-43-5, Piperonyl chloride 24211-54-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of homochiral piperidine derivs. from S-glutamic acid via
stereoselective 1,4-addition of organocuprates to a Δ^3 -piperidine-2-
one in preparation of paroxetine analog)

L1 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1994:595833 CAPLUS
DN 121:195833
TI Antidepressant-induced modulation of GABAA receptors and
 β -adrenoceptors but not GABAB receptors in the frontal cortex of
olfactory bulbectomized rats
AU Dennis, Trevor; Beauchemin, Valerie; Lavoie, Normand
CS Neurobiological Psychiatry Unit, McGill University, Department of
Psychiatry, 1033 Pine Avenue West, Montreal, Quebec, Can.
SO European Journal of Pharmacology (1994), 262(1-2), 143-8
CODEN: EJPHAZ; ISSN: 0014-2999
DT Journal
LA English
AB The effects of prolonged administration of antidepressant drugs, belonging
to three different classes, on high-affinity GABAA receptor, GABAB
receptor and β -adrenoceptor binding parameters were determined in the
frontal cortex of olfactory bulbectomized rats. Clorgyline (1 mg/kg/day),
paroxetine (10 mg/kg/day) or desipramine (10 mg/kg/day) were
administered for 21 days via s.c. osmotic minipumps implanted in the
scapular region 7 days after bulbectomy. Cortical GABAA receptor
densities, defined with [3 H] γ -aminobutyric acid ([3 H]GABA), were
significantly increased following bulbectomy. This effect on Bmax values
was reversed by all three antidepressant drugs. GABAB receptor densities
decreased slightly after bulbectomy. Chronic antidepressant
administration had no effect on GABAB receptor binding parameters.
Olfactory bulbectomy did not induce any changes in cortical
 β -adrenoceptor binding parameters determined with [3 H]CGP-12177
((-)-4-(3-t-butylamino-2-hydroxypropoxy)-[5,7- 3 H]benzimidazol-2-
one). However, prolonged administration of all three antidepressant drugs
induced a downregulation of β -adrenoceptors. The results of the
present study confirm the involvement of cortical GABAA rather than GABAB
receptors in the olfactory bulbectomy animal model of human depression.
Moreover, the data further support the hypothesis that a decrease in
function of the GABAA receptor complex could play a role in the
therapeutic effects of antidepressant treatments.

L1 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1994:525100 CAPLUS
DN 121:125100
TI Further evidence for the importance of 5-HT $_{1A}$ autoreceptors in the action
of selective serotonin reuptake inhibitors
AU Hjorth, Stephan; Auerbach, Sidney B.
CS Department of Pharmacology, University of Goeteborg, Goteborg, Swed.
SO European Journal of Pharmacology (1994), 260(2-3), 251-5
CODEN: EJPHAZ; ISSN: 0014-2999
DT Journal
LA English
AB The clin. efficacy of antidepressants that block serotonin

tartaric acid

(5-hydroxytryptamine, 5-HT) reuptake may be restrained by indirect activation of autoreceptors. In vivo microdialysis in rat hippocampus was used to assess the release-inhibitory properties of the 5-HT reuptake inhibitors citalopram and paroxetine. When reuptake was first blocked by infusing citalopram into the hippocampus, systemic administration of citalopram or paroxetine resulted in a 50-70% decrease in hippocampal 5-HT overflow. This presumably reflected the inhibition of 5-HT release subsequent to reuptake blockade in the raphe nuclei and, in turn, activation of somatodendritic autoreceptors. In support, pretreatment with (\pm)-pindolol or (+)-WAY100135 ((+)-N-tert-butyl-3-(4-(2-methoxyphenyl)piperazine-1-yl)-2-phenylpropanamide dihydrochloride), to block 5-HT_{1A} autoreceptors, abolished the decrease in 5-HT produced by systemic injection of the uptake blockers.

tartaric acid

=> s wo2004026861/pn
L2 1 WO2004026861/PN
(WO2004026861/PN)

=> d bib abs

L2 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:267324 CAPLUS
DN 140:287369
TI Process for producing paroxetine hydrochloride hydrate
IN Yamazaki, Shigeya; Yoshikawa, Taichi
PA Sumika Fine Chemicals Co., Ltd., Japan
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004026861	A1	20040401	WO 2003-JP11806	20030917 <--
	W:			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW	
	RW:			GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG	
	CA 2496727	A1	20040401	CA 2003-2496727	20030917
	AU 2003271056	A1	20040408	AU 2003-271056	20030917
	EP 1555263	A1	20050720	EP 2003-751271	20030917
	R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK	
	BR 2003014596	A	20050809	BR 2003-14596	20030917
	US 2006041138	A1	20060223	US 2005-527337	20050310
PRAI	JP 2002-273901	A	20020919		
	JP 2002-288640	A	20021001		
	WO 2003-JP11806	W	20030917		
AB	This document discloses a process for producing paroxetine hydrochloride hydrate (I), which comprises reacting (3S,4R)-1-tert-butoxycarbonyl-4-(4-fluorophenyl)-3-[(3,4-methylenedioxy)phenoxyethyl]piperidine with hydrogen chloride in the presence of water and then precipitating crystals in the presence of water. Also claimed is a pharmaceutical composition containing I for treatment of a variety of mental disorders.				
RE.CNT	15	THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD			
		ALL CITATIONS AVAILABLE IN THE RE FORMAT			

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ENTER DISPLAY CODE (TI) OR ?:rn
L3 ANALYZE L2 1 RN : 5 TERMS

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COST IN U.S. DOLLARS	ENTRY	SESSION
FULL ESTIMATED COST	16.51	62.64

tartaric acid

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.78	-9.36

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DICTIONARY FILE UPDATES: 12 NOV 2007 HIGHEST RN 953132-99-5

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on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

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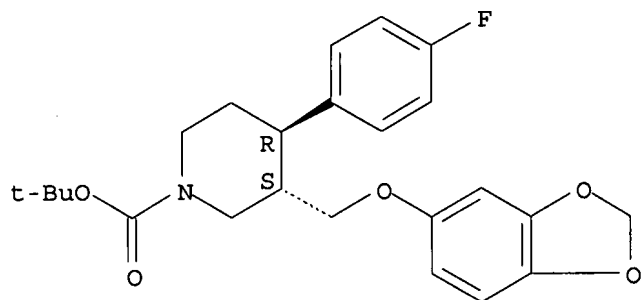
L4 5 L3

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L4 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2007 ACS on STN
RN 200572-35-6 REGISTRY
ED Entered STN: 29 Jan 1998
CN 1-Piperidinecarboxylic acid, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-
fluorophenyl)-, 1,1-dimethylethyl ester, (3S,4R)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1-Piperidinecarboxylic acid, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-
fluorophenyl)-, 1,1-dimethylethyl ester, (3S-trans)-
OTHER NAMES:
CN (3S,4R)-3-[(1,3-Benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-1-
piperidinecarboxylic acid 1,1-dimethylethyl ester
FS STEREOSEARCH
MF C24 H28 F N O5
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).

tartaric acid



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

13 REFERENCES IN FILE CA (1907 TO DATE)

13 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L4 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2007 ACS on STN

RN 110429-35-1 REGISTRY

ED Entered STN: 27 Sep 1987

CN Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, hydrochloride, hydrate (2:2:1), (3S,4R)- (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, hydrochloride, hydrate (2:1), (3S-trans)-

CN Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, hydrochloride, hydrate (2:1), (3S,4R)- (9CI)

OTHER NAMES:

CN (-)-trans-4-(4-Fluorophenyl)-3-(3,4-methylenedioxyphenoxymethyl)piperidine hydrochloride hemihydrate

CN Paroxetine hydrochloride hemihydrate

FS STEREOSEARCH

MF C19 H20 F N O3 . Cl H . 1/2 H2 O

CI COM

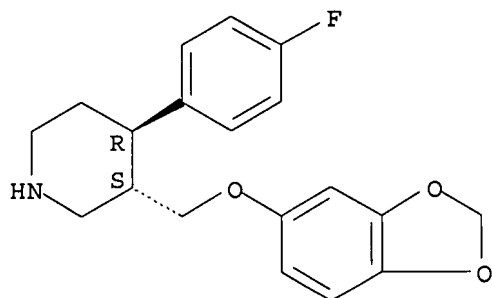
SR CA

LC STN Files: BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, IMSPATENTS, IMSRESEARCH, MRCK*, PS, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

CRN (61869-08-7)

Absolute stereochemistry. Rotation (-).

tartaric acid



● HCl

● 1/2 H₂O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

58 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
58 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L4 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2007 ACS on STN
RN 7732-18-5 REGISTRY
ED Entered STN: 16 Nov 1984
CN Water (CA INDEX NAME)
OTHER NAMES:
CN Aquafina
CN Distilled water
CN DRiWATER
CN Hydrogen oxide (H₂O)
CN NSC 147337
CN R 718
CN Spa
DR 558440-22-5, 558440-53-2
MF H₂ O
CI COM
LC STN Files: ANABSTR, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CSChem, CSNB, DETHERM*, EMBASE, GMELIN*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, PIRA, PROMT, RTECS*, SCISEARCH, SPECINFO, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

H₂O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

398819 REFERENCES IN FILE CA (1907 TO DATE)
1380 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

tartaric acid

399673 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L4 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2007 ACS on STN
RN 7647-01-0 REGISTRY
ED Entered STN: 16 Nov 1984
CN Hydrochloric acid (CA INDEX NAME)
OTHER NAMES:
CN Anhydrous hydrochloric acid
CN Baume HCL
CN Chloridric acid
CN Chlorohydric acid
CN Dilute hydrochloric acid
CN Enplate PO 236
CN Hydrochloric acid gas
CN Hydrogen chloride
CN Hydrogen chloride (HCl)
CN Muriatic acid
CN NSC 77365
DR 113962-65-5, 51005-19-7, 61674-62-2, 218625-68-4
MF Cl H
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BIOSIS, BIOTECHNO, CA,
CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST,
CHEMSAFE, CIN, CSCHEM, CSNB, DETHERM*, EMBASE, ENCOMPLIT, ENCOMPLIT2,
ENCOMPPAT, ENCOMPPAT2, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA,
MEDLINE, MRCK*, MSDS-OHS, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER,
TULSA, ULIDAT, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

HCl

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

105978 REFERENCES IN FILE CA (1907 TO DATE)
654 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
106663 REFERENCES IN FILE CAPLUS (1907 TO DATE)
40 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L4 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2007 ACS on STN
RN 108-88-3 REGISTRY
ED Entered STN: 16 Nov 1984
CN Benzene, methyl- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Toluene (8CI)
OTHER NAMES:
CN 1-Methylbenzene
CN Antisal 1a
CN CP 25
CN CP 25 (solvent)
CN Methacide
CN Methylbenzene
CN Methylbenzol
CN NSC 406333
CN Phenylmethane
CN Toluol
MF C7 H8
CI COM

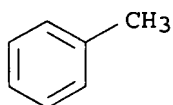
tartaric acid

LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, PIRA, PROMT, PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, ULIDAT, USPAT2, USPATFULL, VETU

(*File contains numerically searchable property data)

Other Sources: DSL**, EINECS**, TSCA**

(**Enter CHEMLIST File for up-to-date regulatory information)



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971 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

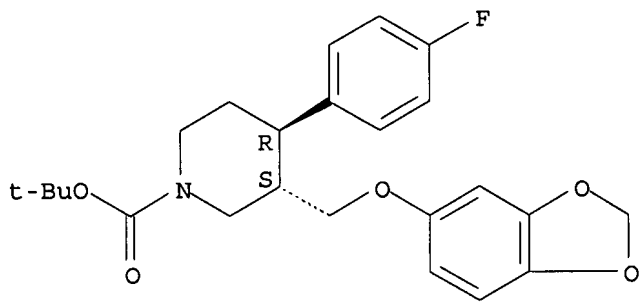
93937 REFERENCES IN FILE CAPLUS (1907 TO DATE)

24 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

tartaric acid

L8 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 200572-35-6 REGISTRY
ED Entered STN: 29 Jan 1998
CN 1-Piperidinecarboxylic acid, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, 1,1-dimethylethyl ester, (3S,4R)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1-Piperidinecarboxylic acid, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, 1,1-dimethylethyl ester, (3S-trans)-
OTHER NAMES:
CN (3S,4R)-3-[(1,3-Benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-1-piperidinecarboxylic acid 1,1-dimethylethyl ester
FS STEREOSEARCH
MF C24 H28 F N O5
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

13 REFERENCES IN FILE CA (1907 TO DATE)
13 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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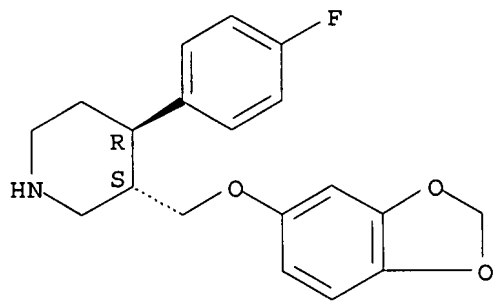
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L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 110429-35-1 REGISTRY
ED Entered STN: 27 Sep 1987
CN Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, hydrochloride, hydrate (2:2:1), (3S,4R)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, hydrochloride, hydrate (2:1), (3S-trans)-
CN Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, hydrochloride, hydrate (2:1), (3S,4R)- (9CI)
OTHER NAMES:
CN (-)-trans-4-(4-Fluorophenyl)-3-(3,4-methylenedioxyphenoxymethyl)piperidine hydrochloride hemihydrate
CN Paroxetine hydrochloride hemihydrate
FS STEREOSEARCH
MF C19 H20 F N O3 . C1 H . 1/2 H2 O
CI COM

• tartaric acid

SR CA
LC STN Files: BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, IMSPATENTS,
IMSRESEARCH, MRCK*, PS, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
CRN (61869-08-7)

Absolute stereochemistry. Rotation (-).



● HCl

● 1/2 H₂O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

58 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
58 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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